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Prussian Blue: Colours and Therapeutic Aspects

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Abstract
The subject of this thesis is the description of the therapeutic aspects of Prussian blue towards heavy metal poisoning (Cs, Tl, radioactive).A remarkable example occurred recently in Italy (2015), as the water in Pietrasanta (Toscana) was found to be contaminated with thallium [1] [2] [3].Prussian blue has different chemical names, including: ferric ferrocyanide, ferrous ferricyanide, hexacyanoferrate (II) to iron (III) hexacyanoferrate (III) to iron (II), and ferric hexacyanoferrate. It is an intense blue pigment and tends towards black or dark purple when mixed with other oil colours.Prussian blue has been described with 2 forms, the soluble, KFe (II) [Fe (III) (CN) 6] and the insoluble form, Fe (III) 4 [Fe (II) (CN) 6] 3 · 6H2O; the name comes from historical reasons rather than by solubility connotations. Keggin and Miles suggested a face-centered cubic structure in which the high-iron spin and low-spin ferrocyanide are arranged in an octahedral structure linked to -NC and -CN units respectively with K + counter ion interstitial site. It lacks a quarter of hexacyanoferrate ions with the nitrogen site occupied instead by a cluster of water molecules coordinated to the site of the Fe (III) with other molecules of interstitial water.It is obtained by reaction between the potassium ferrocyanide and iron (III) ions; the colour is so intense and characteristic as to render this reaction suitable for the detection of iron or cyanides.The Prussian blue can also be used as a chelating agent and in the treatment for heavy metal poisoning, in particular it is used for patients who have ingested radioactive cesium or thallium (or even for the non-radioactive thallium) [4] [5].
Keywords: Prussian blue, Cesium, Thallium, Radioactive.

1. Introduction

The intense blue of Prussian blue is caused by the transfer of electrons from one atom of iron to another within the molecule.

Light is absorbed at 680 nm (red), causing the transfer of an electron from an atom of Fe (II) to a nearby one of Fe (III), the transmitted light is blue.

Despite the presence of cyanide ion, Prussian blue, as other ferrocyanides, is not particularly toxic because of the strong bond between the cyanide ions and iron. However, if treated with concentrated strong acids may liberate cyanide in the form of hydrogen cyanide (better known as hydrocyanic acid), which is extremely toxic.

As "blue of the engineers" is mixed with an oily material, and rubbed on a metal surface.

This in turn is rubbed with another surface, abutment, and the removal of the pigment indicates the position of the points in relief.

Then it can be used to indicate the regularity of a surface or a support.

Prussian blue (insoluble) is used for the treatment of known or suspected internal contamination with radioactive cesium in adults, adolescents, and pediatric patients 2 years of age or older, following known or suspected accidental exposure to these metals and/or intentional exposure from radioactive terrorism or warfare.

Prussian blue increases the rate of elimination of cesium in individuals exposed to potentially toxic amounts of radioactive cesium (137) Cs, as may occur following accidental exposure to or intentional release of this radionuclide.

Contamination with (137) Cs is of particular concern because (137) Cs is a potential component of a radiologic dispersal device (dirty bomb) and is a principal constituent of radioactive fallout.

I've been following the case of two Iraqi men poisoned with thallium.

Because of the hair loss, the head should be shaved since the alopecia is tractional, this assists recovery of hair growth.

They were treated with Prussian blue and 20 years after the recovery they are able to carry out a normal life.

2. Synthesis of Prussian Blue

2.1 Materials

In laboratory: 5 beakers, 10 test tubes, 4 crucibles, Bunsen burner, asbestos sieve, 5 filters, 5 filtrating installations, microbalance.

Chemical substances:

potassium ferrocyanide crystals, $K_4[Fe(CN)_6]$.

FeCl solution, Fe (III).

alkaline chlorine $KClO_3$

hydrochloric acid HCl
distilled water

2.2 Method

Laboratory: preparation of Prussian blue and separation by heating and filtration.
In one beaker, 50 mg of potassium ferrocyanide $K_4[Fe(CN)_6]$ into 100 ml water (stock solution)
Prepare 500 ml of $FeCl_3$ in another beaker (reddish-yellow colour)
The stock solution $K_4[Fe(CN)_6]$ is to be divided between 2 test tubes, each one will contain 20ml. Put enough $FeCl_3$ for the precipitate to appear in both test tubes.
The change of colour is immediate: put the solution from one of the test tubes in the crucible on the asbestos sieve, light the Bunsen burner, let it heat for a few (5-10) minutes and then observe the solid formed.
The procedure is repeated in order to achieve a higher precision.
The chemical equation on which the reaction is based is:
$4FeCl_3 + 3K_4[Fe(CN)_6] \rightarrow Fe_4[Fe(CN)_6] + 12KCl$
The direct precipitation method

$$2\ FeCl_2 + K_4\ [Fe(CN)_6] \rightarrow Fe_2\ [Fe\ (CN)_6] + 4\ KCl$$
$$3\ Fe_2\ [Fe\ (CN)_6] + KClO_3 + 6\ HCl \rightarrow$$
$$\rightarrow Fe_4\ [Fe\ (CN)_6\ ]_3 + 2\ FeCl_2 + KCl + 3\ H_2\ O + Cl_2$$

Another procedure: filtration
Prepare the filtering installation and then put the solution from the test tube on the beaker.

3. Analytical Applications

The participation of cations in redox reaction of metal hexacyanoferrates provides a unique opportunity for development of chemical sensors for nonelectroactive ions. The development of sensors for thallium (Tl^+) [14], cesium (Cs^+) and potassium (K^+) pioneered the analytical applications of metal hexacyanoferrates.

4. Therapeutic Uses (chelation therapy)

Prussian blue insoluble is indicated for the treatment of patients with known or suspected internal contamination with radioactive cesium and /or radioactive or non-radioactive thallium to increase their rates of elimination [6].

In a 1987 incident in Goiania, Brazil, 46 persons with heavy internal contamination with 137-cesium (137-Cs) were treated with Prussian blue insoluble [7].

Data on the whole body effective half-life of 137-Cs, during and after Prussian blue insoluble treatment was completed on 33/46 of these patients.

Hexacyanoferrate compounds (commonly referred to as Prussian blue) are highly effective radiocesium binders [8].

They may be added to the diet of dairy cows, sheep, goats, as well as to meat producing animals, to reduce radiocesium transfer to milk and meat by reducing absorption in the gut.

4.1 Drug Warning

Prussian blue insoluble is administered to decrease radiation exposure.
It does not treat the complications of radiation exposure. Patients contaminated with doses of 137 – Cs may develop radiation toxicity including bone marrow suppression with severe neutropenia thrombocytopenia [9].
In patients who cannot swallow capsules, when the capsules are opened and the contents are mixed with food and eaten, the mouth and teeth might be coloured blue [10].

Prussian blue insoluble may bind electrolytes found in the gastrointestinal tract. Asymptomatic hypokalemia, with serum potassium values of 2.5–2.9 (normal 3.5 – 5.0), was reported in 3/42 (7%) of patients on treatment with Prussian blue insoluble.

Binding to some therapeutic drugs and essential nutrients is possible. The literature contains anecdotal reports of asymptomatic hypokalemia and decreased bioavailability of oral tetracycline [11].

Histopathological examination of different organs showed no deposits of Prussian blue after oral administration of insoluble Prussian blue [12].

Prussian blue is an orally administered insoluble unabsorbable molecule that exchanges potassium ions for thallium in gut lumen. Prussian blue blocks the enterohepatic and enteroenteric recirculation of thallium, increasing fecal elimination. It has been shown to decrease the elimination half-life of thallium, from 8 to 3 days and to decrease mortality in an animal model [13].

5. Results, Discussion

The exact mechanism of toxicity of cesium and thallium isn't clear. Another toxic mechanism is the interference with riboflavin (vitamin b2) homeostasis through the formation of insoluble complexes and the intracellular sequestration of riboflavin. The deficiency of this vitamin causes dermatitis, alopecia and neuropathy. Skin lesions similar to those occurring in riboflavin deficiency have been described in thallium poisoning.

Prussian blue insoluble acts by ion-exchange, adsorption, and mechanical trapping within the crystal structure and has a very high affinity for radioactive and non-radioactive cesium and thallium.

Prussian blue is unlikely to distribute into breast milk. Because cesium and thallium are distributed into human breast milk, women contaminated with these metals should not breast-feed infants.

Prussian blue does not undergo hepatic metabolism; use of the drug is not contra indicated in patients with hepatic impairment.

6. Conclusions

If the patient presents within 4 hours, immediate treatment consists of gastric lavage followed by instillation of Prussian blue. Bear in mind that thallium is radio-opaque, so that ingestion can be confirmed by abdominal X-ray.

Daily urea, creatinine and electrolyte measurements, especially potassium as Prussian blue therapy may result in hypokalaemia. Initial measurements of Mg, Ca, phosphate, amylase, CPK and liver function tests. Hypokalaemia has been reported.

Dose: Oral Capsules, 500 mg in one capsule; Radiogardase, Heyl Chem.- pharm. Fabrik GmbH& Co. KG [15]. It is recommended the giving of the dose under clinical control, with a dietary supplement, food rich in complex vitamins and other necessary elements K, Na, Ca Fe, proteins, fibre-rich food to enhance intestinal motility.

Among the consequences of thallium poisoning there is reversible alopecia (Fig.2). After the treatment with Prussian blue, hair growth is a sign of recovery.

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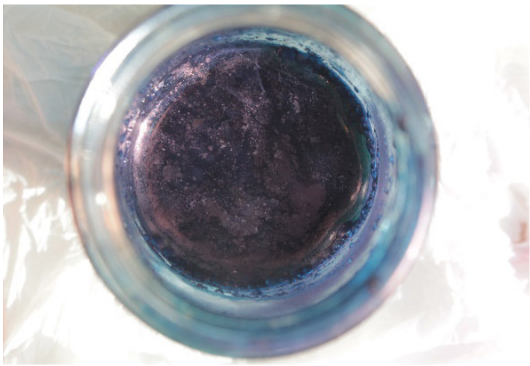

Figure 1 Prussian blue

Figure 2 Alopecia

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